DETAILED ACTION

Applicant's amendment and response of 4/14/08 are entered.

Claim 9 is amended.

Claims 10 and 14 are cancelled.

Claims 46-48 are newly presented.

Claims 9, 15, 16, 34 and 40-48 are presently pending and considered.

Claim Status, Cancelled Claims

In light of the cancellation of Claims 10 and 14, all rejections and/or objections to such claims are rendered moot, and thus, are withdrawn.

Non-Finality of Present Action

The Examiner notes that, contrary to Applicant's argument, former claim 14 was substantively rejected; however, as the form paragraph did not list Claim 14, due to typographical error, the present action is made non-final.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The

filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

In light of the cancellation of Claim 10, the advisory that should 10 be found allowable, claims 41 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof, is rendered moot, and thus, is withdrawn.

35 USC 112, first paragraph – Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

In light of the amendments, the rejections of Claims 9-10, 14-16, and 34 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for direct administration to the site proximal to the lymphnode, does not reasonably provide enablement for any method of delivery which transforms macrophage cells at the site, are withdrawn.

To wit, the amendments no longer allow the methods to encompass the broader genera of administrations routes which was rejected.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 9, 15-16, 34, and 40-45 remain rejected, and Claims 46-48 are newly rejected, under 35 U.S.C. 103(a) as being unpatentable over US PAT APP NO 2004/0063652 to Jolly, Kataoka, et al. (1997) J. Biol. Chem., 272(29): 18209-15, US PAT NO 5,783,567 to Hedley, et al., Samlowski, et al. (1988) Regional Immunology, 1(1): 41-55, US PAT NO 5,763,416 to Bonadio, et al, for reasons of record as necessitated by the amendments.

Jolly teaches the use of plasmids (e.g., paragraph 0037) to effect the transformation of macrophage cells, to effect killing (e.g., paragraphs 0067-71) and for general secretion of proteins that block pathogenic interactions local to the cell (paragraph 0155), which requires secretion signals.

Kataoka teaches the human CD156 gene, and its promoter sequence as specific for macrophage expression, as well as the structure of such promoters (p. 18215).

Hedley teaches the transformation of macrophages of the draining lymph nodes by subcutaneous injection (e.g., col. 8, paragraph 3), and Samlowski teaches that macrophages were known to drain to the lymph nodes local to the site of injection (e.g., ABSTRACT), hence, macrophages drain locally and not distantly.

Bonadio teaches that the SV40 polyA signal is a standard signal for termination of transcripts (e.g., EXAMPLE IX).

From the confluence of this, it is clear that Jolly teaches transfection of macrophages *in vivo* with plasmids, Hedley and Samlowski teaches that transformation of the macrophages will lead to transfected cells in the draining lymph nodes, and Kataoka and Bonadio teach the required signals for expression of a gene in macrophages.

Further, when injecting substances, it is standard in the Art to administer substances which numb the area to avoid hurting the subject. One such substance which is well known in the Art is Bupivacaine (Attached http://www.drugdigest.org/DD/DVH/Uses/0,3915,7903%7CBupivacaine%2BHCL,00.html). Hence, the further administration of Bupivacaine was well known in the Art for such use, and as such the further utilization of Bupivacaine would be obvious.

Therefore, at the time of invention, the method would have been obvious. The Artisan would choose a site local to the lymph node target, which may be intramuscular, intradermal, subcutaneous, or intraperitoneal, depending on which lymph nodes are being targeted (it is well known in the Art that lymph nodes are located throughout the body and near each of these sites) because the macrophages were known to drain to local lymph nodes. Still further, the Artisan would inject the plasmid by IM injection in order to deliver it to a lymph node local to the muscle injection site. Still further, the administration of Bupivacaine to a subject during or prior to injection of the vector would be motivated in order to avoid pain in the subject due to administration. Moreover, the Artisan would have expected success, as the transformation of macrophages was already well known and the draining of such macrophages to lymph nodes was well known in the Art. In addition, the obtained result would necessarily be obtained as the macrophage is secreting the protein.

Arguments of specific motivation are now precluded by KSR v. Teleflex. In essence, Applicant's claims reflect what is already known in the Art to occur and is simply another method that the Artisan would be capable of performing prior to the invention in order to get proteins into the lymph nodes. In addition, without a requirement of the amounts of protein or

some other limitation such that the Artisan would not expect it to work, there is a reasonable expectation of success.

For purposes of speeding an anticipated appeal, the following explanation is provided. The methods of the invention center around the administration of a vector to a tissue in order to transform and express a protein from macrophages, which protein is then secreted by the macrophage. The macrophage subsequently drains into a local lymph node, thereby providing the protein to the lymph node in the form of its secretion from the macrophage. The Art demonstrates that the methods of transforming macrophages, the use of promoters specific for macrophages to effect their tissue-specific expression in macrophages, the use of secretion signals, and the use of the polyA tails was well known in the Art. Still further, and critically, the Art recognized that macrophages drained into lymph nodes local to their tissue site, as shown in Samlowski. The question then, appears to the Examiner to be whether or not the Artisan would have been able to put together these functions and utilize them derive a method encompassed by the claims. The Examiner maintains that this knowledge is within the skill of the Artisan, and the non-specific motivation is the combined knowledge in the Art that the macrophages drain to local lymph nodes, with the known mechanisms of causing the macrophages to secrete a protein.

Response to Argument – obviousness

Applicant's argument of 4/14/08 states that Claim 9 has been amended to encompass Claim 14, and as such, because the form paragraph did not indicate rejection of such claim, the claims are free of the prior art.

Such is not persuasive. The Examiner, as noted above, did substantially reject the claim, but due to typographical error, missed putting such claim in the form paragraph. Hence, the claims remain rejected, as due to the amendments.

CONCLUSION

No Claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT M. KELLY whose telephone number is (571)272-0729. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Robert M Kelly/
Primary Examiner of Art Unit 1633